

ATTORNEY DOCKET NUMBER: M0765/7038/ERG/KA
Express Mail Label No.: EL844533645US
Date of Deposit: November 1, 2001

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicants: David T. Scadden, et al.
Serial No. Not Yet Assigned
Filed: November 1, 2001
For: THE CaR RECEPTOR AS A MEDIATOR OF MIGRATORY CELL
CHEMOTAXIS AND/OR CHEMOKINESIS
Examiner: Not Yet Assigned
Art Unit: Not Yet Assigned

BOX PATENT APPLICATION
COMMISSIONER FOR PATENTS
WASHINGTON, D.C. 20231

Sir:

STATEMENT PURSUANT TO 37 C.F.R. §1.821(f)

This statement is made pursuant to 37 C.F.R. §1.821(f). Applicants enclose herewith an original written copy of the Sequence Listing and a computer readable diskette. Applicants' representative states that the information recorded in the computer readable form is identical to the written Sequence Listing and that the Sequence Listing contains no new matter.

Respectfully submitted,

Konstantinos Andrikopoulos

Konstantinos Andrikopoulos, Reg. No. 48,915
WOLF, GREENFIELD & SACKS, P.C.
600 Atlantic Avenue
Boston, MA 02210-2211
(617)720-3500

Attorney's Doc. No.: M0765/7038 (ERG/KA)
November 1, 2001
xNDD

SEQUENCE LISTING

<110> Scadden, David T.
Poznansky, Mark C.
Olszak, Ivona T.
Brown, Edward M.

<120> THE CaR RECEPTOR AS A MEDIATOR OF MIGRATORY CELL CHEMOTAXIS
AND/OR CHEMOKINESIS

<130> M0765/7038/ERG/KA

<150> PCT/US00/15440

<151> 2000-06-02

<160> 2

<170> FastSEQ for Windows Version 3.0

<210> 1

<211> 3361

<212> DNA

<213> Homo sapiens

<220>

<221> CDS

<222> (29)...(3262)

<223> Ca-sensing Receptor

<400> 1

| | |
|---|-----|
| tcccttgccc tggagagacg gcagaacc atg gca ttt tat agc tgc tgc tgg | 52 |
| Met Ala Phe Tyr Ser Cys Cys Trp | |
| 1 5 | |
| gtc ctc ttg gca ctc acc tgg cac acc tct gcc tac ggg cca gac cag | 100 |
| Val Leu Leu Ala Leu Thr Trp His Thr Ser Ala Tyr Gly Pro Asp Gln | |
| 10 15 20 | |
| cga gcc caa aag aag ggg gac att atc ctt ggg ggg ctc ttt cct att | 148 |
| Arg Ala Gln Lys Lys Gly Asp Ile Ile Leu Gly Gly Leu Phe Pro Ile | |
| 25 30 35 40 | |
| cat ttt gga gta gca gct aaa gat caa gat ctc aaa tca agg ccg gag | 196 |
| His Phe Gly Val Ala Ala Lys Asp Gln Asp Leu Lys Ser Arg Pro Glu | |
| 45 50 55 | |
| tct gtg gaa tgt atc agg tat aat ttc cgt ggg ttt cgc tgg tta cag | 244 |
| Ser Val Glu Cys Ile Arg Tyr Asn Phe Arg Gly Phe Arg Trp Leu Gln | |
| 60 65 70 | |
| gct atg ata ttt gcc ata gag gag ata aac agc agc cca gcc ctt ctt | 292 |
| Ala Met Ile Phe Ala Ile Glu Glu Ile Asn Ser Ser Pro Ala Leu Leu | |
| 75 80 85 | |
| ccc aac ttg acg ctg gga tac agg ata ttt gac act tgc aac acc gtt | 340 |
| Pro Asn Leu Thr Leu Gly Tyr Arg Ile Phe Asp Thr Cys Asn Thr Val | |
| 90 95 100 | |
| tct aag gcc ttg gaa gcc acc ctg agt ttt gtt gct caa aac aaa att | 388 |
| Ser Lys Ala Leu Glu Ala Thr Leu Ser Phe Val Ala Gln Asn Lys Ile | |
| 105 110 115 120 | |

10002354-110101

| | |
|---|------|
| gat tct ttg aac ctt gat gag ttc tgc aac tgc tca gag cac att ccc | 436 |
| Asp Ser Leu Asn Leu Asp Glu Phe Cys Asn Cys Ser Glu His Ile Pro | |
| 125 130 135 | |
| tct acg att gct gtg gtg gga gca act ggc tca ggc gtc tcc acg gca | 484 |
| Ser Thr Ile Ala Val Val Gly Ala Thr Gly Ser Gly Val Ser Thr Ala | |
| 140 145 150 | |
| gtg gca aat ctg ctg ggg ctc ttc tac att ccc cag gtc agt tat gcc | 532 |
| Val Ala Asn Leu Leu Gly Leu Phe Tyr Ile Pro Gln Val Ser Tyr Ala | |
| 155 160 165 | |
| tcc tcc agc aga ctc ctc agc aac aag aat caa ttc aag tct ttc ctc | 580 |
| Ser Ser Ser Arg Leu Leu Ser Asn Lys Asn Gln Phe Lys Ser Phe Leu | |
| 170 175 180 | |
| cga acc atc ccc aat gat gag cac cag gcc act gcc atg gca gac atc | 628 |
| Arg Thr Ile Pro Asn Asp Glu His Gln Ala Thr Ala Met Ala Asp Ile | |
| 185 190 195 200 | |
| atc gag tat ttc cgc tgg aac tgg gtg ggc aca att gca gct gat gac | 676 |
| Ile Glu Tyr Phe Arg Trp Asn Trp Val Gly Thr Ile Ala Ala Asp Asp | |
| 205 210 215 | |
| gac tat ggg cgg ccg ggg att gag aaa ttc cga gag gaa gct gag gaa | 724 |
| Asp Tyr Gly Arg Pro Gly Ile Glu Lys Phe Arg Glu Glu Ala Glu Glu | |
| 220 225 230 | |
| agg gat atc tgc atc gac ttc agt gaa ctc atc tcc cag tac tct gat | 772 |
| Arg Asp Ile Cys Ile Asp Phe Ser Glu Leu Ile Ser Gln Tyr Ser Asp | |
| 235 240 245 | |
| gag gag gag atc cag cat gtg gta gag gtg att caa aat tcc acg gcc | 820 |
| Glu Glu Glu Ile Gln His Val Val Glu Val Ile Gln Asn Ser Thr Ala | |
| 250 255 260 | |
| aaa gtc atc gtg gtt ttc tcc agt ggc cca gat ctt gag ccc ctc atc | 868 |
| Lys Val Ile Val Val Phe Ser Ser Gly Pro Asp Leu Glu Pro Leu Ile | |
| 265 270 275 280 | |
| aag gag att gtc cgg cgc aat atc acg ggc aag atc tgg ctg gcc agc | 916 |
| Lys Glu Ile Val Arg Arg Asn Ile Thr Gly Lys Ile Trp Leu Ala Ser | |
| 285 290 295 | |
| gag gcc tgg gcc agc tcc tcc ctg atc gcc atg cct cag tac ttc cac | 964 |
| Glu Ala Trp Ala Ser Ser Ser Leu Ile Ala Met Pro Gln Tyr Phe His | |
| 300 305 310 | |
| gtg gtt ggc ggc acc att gga ttc gct ctg aag gct ggg cag atc cca | 1012 |
| Val Val Gly Gly Thr Ile Gly Phe Ala Leu Lys Ala Gly Gln Ile Pro | |
| 315 320 325 | |
| ggc ttc cgg gaa ttc ctg aag aag gtc cat ccc agg aag tct gtc cac | 1060 |
| Gly Phe Arg Glu Phe Leu Lys Lys Val His Pro Arg Lys Ser Val His | |
| 330 335 340 | |
| aat ggt ttt gcc aag gag ttt tgg gaa gaa aca ttt aac tgc cac ctc | 1108 |
| Asn Gly Phe Ala Lys Glu Phe Trp Glu Glu Thr Phe Asn Cys His Leu | |
| 345 350 355 360 | |
| caa gaa ggt gca aaa gga cct tta cct gtg gac acc ttt ctg aga ggt | 1156 |

10002854-110101

| | | | | | | | | | | | | | | | | | |
|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|--|------|
| Gln | Glu | Gly | Ala | Lys | Gly | Pro | Leu | Pro | Val | Asp | Thr | Phe | Leu | Arg | Gly | | |
| | | | | 365 | | | | | 370 | | | | | 375 | | | |
| cac | gaa | gaa | agt | ggc | gac | agg | ttt | agc | aac | agc | tcg | aca | gcc | ttc | cga | | 1204 |
| His | Glu | Glu | Ser | Gly | Asp | Arg | Phe | Ser | Asn | Ser | Ser | Thr | Ala | Phe | Arg | | |
| | | | 380 | | | | | 385 | | | | | 390 | | | | |
| ccc | ctc | tgt | aca | ggg | gat | gag | aac | atc | agc | agt | gtc | gag | acc | cct | tac | | 1252 |
| Pro | Leu | Cys | Thr | Gly | Asp | Glu | Asn | Ile | Ser | Ser | Val | Glu | Thr | Pro | Tyr | | |
| | | 395 | | | | | 400 | | | | | 405 | | | | | |
| ata | gat | tac | acg | cat | tta | cgg | ata | tcc | tac | aat | gtg | tac | tta | gca | gtc | | 1300 |
| Ile | Asp | Tyr | Thr | His | Leu | Arg | Ile | Ser | Tyr | Asn | Val | Tyr | Leu | Ala | Val | | |
| | 410 | | | | | 415 | | | | | 420 | | | | | | |
| tac | tcc | att | gcc | cac | gcc | ttg | caa | gat | ata | tat | acc | tgc | tta | cct | ggg | | 1348 |
| Tyr | Ser | Ile | Ala | His | Ala | Leu | Gln | Asp | Ile | Tyr | Thr | Cys | Leu | Pro | Gly | | |
| 425 | | | | | 430 | | | | | 435 | | | | | 440 | | |
| aga | ggg | ctc | ttc | acc | aat | ggc | tcc | tgt | gca | gac | atc | aag | aaa | gtt | gag | | 1396 |
| Arg | Gly | Leu | Phe | Thr | Asn | Gly | Ser | Cys | Ala | Asp | Ile | Lys | Lys | Val | Glu | | |
| | | | | 445 | | | | | 450 | | | | | 455 | | | |
| gcg | tgg | cag | gtc | ctg | aag | cac | cta | cgg | cat | cta | aac | ttt | aca | aac | aat | | 1444 |
| Ala | Trp | Gln | Val | Leu | Lys | His | Leu | Arg | His | Leu | Asn | Phe | Thr | Asn | Asn | | |
| | | | 460 | | | | | 465 | | | | | 470 | | | | |
| atg | ggg | gag | cag | gtg | acc | ttt | gat | gag | tgt | ggg | gac | ctg | gtg | ggg | aac | | 1492 |
| Met | Gly | Glu | Gln | Val | Thr | Phe | Asp | Glu | Cys | Gly | Asp | Leu | Val | Gly | Asn | | |
| | 475 | | | | | | 480 | | | | | 485 | | | | | |
| tat | tcc | atc | atc | aac | tgg | cac | ctc | tcc | cca | gag | gat | ggc | tcc | atc | gtg | | 1540 |
| Tyr | Ser | Ile | Ile | Asn | Trp | His | Leu | Ser | Pro | Glu | Asp | Gly | Ser | Ile | Val | | |
| | 490 | | | | | 495 | | | | | 500 | | | | | | |
| ttt | aag | gaa | gtc | ggg | tat | tac | aac | gtc | tat | gcc | aag | aag | gga | gaa | aga | | 1588 |
| Phe | Lys | Glu | Val | Gly | Tyr | Tyr | Asn | Val | Tyr | Ala | Lys | Lys | Gly | Glu | Arg | | |
| 505 | | | | | 510 | | | | | 515 | | | | | 520 | | |
| ctc | ttc | atc | aac | gag | gag | aaa | atc | ctg | tgg | agt | ggg | ttc | tcc | agg | gag | | 1636 |
| Leu | Phe | Ile | Asn | Glu | Glu | Lys | Ile | Leu | Trp | Ser | Gly | Phe | Ser | Arg | Glu | | |
| | | | 525 | | | | | | 530 | | | | | 535 | | | |
| gtg | ccc | ttc | tcc | aac | tgc | agc | cga | gac | tgc | ctg | gca | ggg | acc | agg | aaa | | 1684 |
| Val | Pro | Phe | Ser | Asn | Cys | Ser | Arg | Asp | Cys | Leu | Ala | Gly | Thr | Arg | Lys | | |
| | | | 540 | | | | | 545 | | | | | 550 | | | | |
| ggg | atc | att | gag | ggg | gag | ccc | acc | tgc | tgc | ttt | gag | tgt | gtg | gag | tgt | | 1732 |
| Gly | Ile | Ile | Glu | Gly | Glu | Pro | Thr | Cys | Cys | Phe | Glu | Cys | Val | Glu | Cys | | |
| | | 555 | | | | | | 560 | | | | 565 | | | | | |
| cct | gat | ggg | gag | tat | agt | gat | gag | aca | gat | gcc | agt | gcc | tgt | aac | aag | | 1780 |
| Pro | Asp | Gly | Glu | Tyr | Ser | Asp | Glu | Thr | Asp | Ala | Ser | Ala | Cys | Asn | Lys | | |
| | 570 | | | | | 575 | | | | | 580 | | | | | | |
| tgc | cca | gat | gac | ttc | tgg | tcc | aat | gag | aac | cac | acc | tcc | tgc | att | gcc | | 1828 |
| Cys | Pro | Asp | Asp | Phe | Trp | Ser | Asn | Glu | Asn | His | Thr | Ser | Cys | Ile | Ala | | |
| 585 | | | | | 590 | | | | | 595 | | | | | 600 | | |
| aag | gag | atc | gag | ttt | ctg | tcg | tgg | acg | gag | ccc | ttt | ggg | atc | gca | ctc | | 1876 |
| Lys | Glu | Ile | Glu | Phe | Leu | Ser | Trp | Thr | Glu | Pro | Phe | Gly | Ile | Ala | Leu | | |
| | | | | 605 | | | | | 610 | | | | | 615 | | | |

10002854-110101

| | |
|---|------|
| acc ctc ttt gcc gtg ctg ggc att ttc ctg aca gcc ttt gtg ctg ggt | 1924 |
| Thr Leu Phe Ala Val Leu Gly Ile Phe Leu Thr Ala Phe Val Leu Gly | |
| 620 625 630 | |
| gtg ttt atc aag ttc cgc aac aca ccc att gtc aag gcc acc aac cga | 1972 |
| Val Phe Ile Lys Phe Arg Asn Thr Pro Ile Val Lys Ala Thr Asn Arg | |
| 635 640 645 | |
| gag ctc tcc tac ctc ctc ctc ttc tcc ctg ctc tgc tgc ttc tcc agc | 2020 |
| Glu Leu Ser Tyr Leu Leu Leu Phe Ser Leu Leu Cys Cys Phe Ser Ser | |
| 650 655 660 | |
| tcc ctg ttc ttc atc ggg gag ccc cag gac tgg acg tgc cgc ctg cgc | 2068 |
| Ser Leu Phe Phe Ile Gly Glu Pro Gln Asp Trp Thr Cys Arg Leu Arg | |
| 665 670 675 680 | |
| cag ccg gcc ttt ggc atc agc ttc gtg ctc tgc atc tca tgc atc ctg | 2116 |
| Gln Pro Ala Phe Gly Ile Ser Phe Val Leu Cys Ile Ser Cys Ile Leu | |
| 685 690 695 | |
| gtg aaa acc aac cgt gtc ctc ctg gtg ttt gag gcc aag atc ccc acc | 2164 |
| Val Lys Thr Asn Arg Val Leu Leu Val Phe Glu Ala Lys Ile Pro Thr | |
| 700 705 710 | |
| agc ttc cac cgc aag tgg tgg ggg ctc aac ctg cag ttc ctg ctg gtt | 2212 |
| Ser Phe His Arg Lys Trp Trp Gly Leu Asn Leu Gln Phe Leu Leu Val | |
| 715 720 725 | |
| ttc ctc tgc acc ttc atg cag att gtc atc tgt gtg atc tgg ctc tac | 2260 |
| Phe Leu Cys Thr Phe Met Gln Ile Val Ile Cys Val Ile Trp Leu Tyr | |
| 730 735 740 | |
| acc gcg ccc ccc tca agc tac cgc aac cag gag ctg gag gat gag atc | 2308 |
| Thr Ala Pro Pro Ser Ser Tyr Arg Asn Gln Glu Leu Glu Asp Glu Ile | |
| 745 750 755 760 | |
| atc ttc atc acg tgc cac gag ggc tcc ctc atg gcc ctg ggc ttc ctg | 2356 |
| Ile Phe Ile Thr Cys His Glu Gly Ser Leu Met Ala Leu Gly Phe Leu | |
| 765 770 775 | |
| atc ggc tac acc tgc ctg ctg gct gcc atc tgc ttc ttc ttt gcc ttc | 2404 |
| Ile Gly Tyr Thr Cys Leu Leu Ala Ala Ile Cys Phe Phe Phe Ala Phe | |
| 780 785 790 | |
| aag tcc cgg aag ctg ccg gag aac ttc aat gaa gcc aag ttc atc acc | 2452 |
| Lys Ser Arg Lys Leu Pro Glu Asn Phe Asn Glu Ala Lys Phe Ile Thr | |
| 795 800 805 | |
| ttc agc atg ctc atc ttc ttc atc gtc tgg atc tcc ttc att cca gcc | 2500 |
| Phe Ser Met Leu Ile Phe Phe Ile Val Trp Ile Ser Phe Ile Pro Ala | |
| 810 815 820 | |
| tat gcc agc acc tat ggc aag ttt gtc tct gcc gta gag gtg att gcc | 2548 |
| Tyr Ala Ser Thr Tyr Gly Lys Phe Val Ser Ala Val Glu Val Ile Ala | |
| 825 830 835 840 | |
| atc ctg gca gcc agc ttt ggc ttg ctg gcg tgc atc ttc ttc aac aag | 2596 |
| Ile Leu Ala Ala Ser Phe Gly Leu Leu Ala Cys Ile Phe Phe Asn Lys | |
| 845 850 855 | |
| acc tac atc att ctc ttc aag cca tcc cgc aac acc atc gag gag gtg | 2644 |

10002354-10101

| | | | | | | | | | | | | | | | | | |
|------------|------------|------------|------------|-------------|------------|------|-----|------|-----|------|------|------|------|-----|------|------|--|
| Thr | Tyr | Ile | Ile | Leu | Phe | Lys | Pro | Ser | Arg | Asn | Thr | Ile | Glu | Glu | Val | | |
| | | | 860 | | | | | 865 | | | | | 870 | | | | |
| cgt | tgc | agc | acc | gca | cgt | cac | gct | ttc | aag | gtg | gct | gcc | cgg | gcc | acg | 2692 | |
| Arg | Cys | Ser | Thr | Ala | Arg | His | Ala | Phe | Lys | Val | Ala | Ala | Arg | Ala | Thr | | |
| | | 875 | | | | | 880 | | | | | 885 | | | | | |
| ctg | cgc | cgc | agc | aac | gtc | tcc | cgc | aag | cgg | tcc | agc | agc | ctt | gga | ggc | 2740 | |
| Leu | Arg | Arg | Ser | Asn | Val | Ser | Arg | Lys | Arg | Ser | Ser | Ser | Leu | Gly | Gly | | |
| | 890 | | | | | 895 | | | | | 900 | | | | | | |
| tcc | acg | gga | tcc | acc | ccc | tcc | tcc | tcc | atc | agc | agc | aag | agc | aac | agc | 2788 | |
| Ser | Thr | Gly | Ser | Thr | Pro | Ser | Ser | Ser | Ile | Ser | Ser | Lys | Ser | Asn | Ser | | |
| 905 | | | | | 910 | | | | | 915 | | | | | 920 | | |
| gaa | gac | cca | ttc | cca | cag | ccc | gag | agg | cag | aag | cag | cag | cag | ccg | ctg | 2836 | |
| Glu | Asp | Pro | Phe | Pro | Gln | Pro | Glu | Arg | Gln | Lys | Gln | Gln | Gln | Pro | Leu | | |
| | | | | 925 | | | | | 930 | | | | | 935 | | | |
| gcc | cta | acc | cag | caa | gag | cag | cag | cag | cag | ccc | ctg | acc | ctc | cca | cag | 2884 | |
| Ala | Leu | Thr | Gln | Gln | Glu | Gln | Gln | Gln | Gln | Pro | Leu | Thr | Leu | Pro | Gln | | |
| | | | 940 | | | | | 945 | | | | | 950 | | | | |
| cag | caa | cga | tct | cag | cag | cag | ccc | aga | tgc | aag | cag | aag | gtc | atc | ttt | 2932 | |
| Gln | Gln | Arg | Ser | Gln | Gln | Gln | Pro | Arg | Cys | Lys | Gln | Lys | Val | Ile | Phe | | |
| | | 955 | | | | | 960 | | | | | 965 | | | | | |
| ggc | agc | ggc | acg | gtc | acc | ttc | tca | ctg | agc | ttt | gat | gag | cct | cag | aag | 2980 | |
| Gly | Ser | Gly | Thr | Val | Thr | Phe | Ser | Leu | Ser | Phe | Asp | Glu | Pro | Gln | Lys | | |
| | 970 | | | | | 975 | | | | | 980 | | | | | | |
| aac | gcc | atg | gcc | cac | agg | aat | tct | acg | cac | cag | aac | tcc | ctg | gag | gcc | 3028 | |
| Asn | Ala | Met | Ala | His | Arg | Asn | Ser | Thr | His | Gln | Asn | Ser | Leu | Glu | Ala | | |
| 985 | | | | | 990 | | | | | 995 | | | | | 1000 | | |
| cag | aaa | agc | agc | gat | acg | ctg | acc | cga | cac | cag | cca | tta | ctc | ccg | ctg | 3076 | |
| Gln | Lys | Ser | Ser | Asp | Thr | Leu | Thr | Arg | His | Gln | Pro | Leu | Leu | Pro | Leu | | |
| | | | | 1005 | | | | 1010 | | | | | 1015 | | | | |
| cag | tgc | ggg | gaa | acg | gac | tta | gat | ctg | acc | gtc | cag | gaa | aca | ggg | ctg | 3124 | |
| Gln | Cys | Gly | Glu | Thr | Asp | Leu | Asp | Leu | Thr | Val | Gln | Glu | Thr | Gly | Leu | | |
| | | | 1020 | | | | | 1025 | | | | | 1030 | | | | |
| caa | gga | cct | gtg | ggg | gga | gac | cag | cgg | cca | gag | gtg | gag | gac | cct | gaa | 3172 | |
| Gln | Gly | Pro | Val | Gly | Gly | Asp | Gln | Arg | Pro | Glu | Val | Glu | Asp | Pro | Glu | | |
| | | 1035 | | | | 1040 | | | | | | 1045 | | | | | |
| gag | ttg | tcc | cca | gca | ctt | gta | gtg | tcc | agt | tca | cag | agc | ttt | gtc | atc | 3220 | |
| Glu | Leu | Ser | Pro | Ala | Leu | Val | Val | Ser | Ser | Ser | Gln | Ser | Phe | Val | Ile | | |
| | 1050 | | | | | 1055 | | | | | 1060 | | | | | | |
| agt | ggg | gga | ggc | agc | act | gtt | aca | gaa | aac | gta | gtg | aat | tca | | | 3262 | |
| Ser | Gly | Gly | Gly | Ser | Thr | Val | Thr | Glu | Asn | Val | Val | Asn | Ser | | | | |
| 065 | | | | | 1070 | | | | | 1075 | | | | | | | |
| taaaatggaa | ggagaagact | gggctaggga | gaatgcagag | agggtttcttg | gggtcccagg | 3322 | | | | | | | | | | | |
| gatgaggaat | cgccccagac | tcctttcctc | tgaggaaga | | | 3361 | | | | | | | | | | | |

<210> 2
 <211> 1078
 <212> PRT
 <213> Homo sapiens

10002354.10101

<220>
 <221> PEPTIDE
 <222> (1)...(1078)
 <223> Ca-sensing Receptor

<400> 2

| | | | | | | | | | | | | | | | |
|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|
| Met | Ala | Phe | Tyr | Ser | Cys | Cys | Trp | Val | Leu | Leu | Ala | Leu | Thr | Trp | His |
| 1 | | | | 5 | | | | | 10 | | | | | 15 | |
| Thr | Ser | Ala | Tyr | Gly | Pro | Asp | Gln | Arg | Ala | Gln | Lys | Lys | Gly | Asp | Ile |
| | | | 20 | | | | | 25 | | | | | 30 | | |
| Ile | Leu | Gly | Gly | Leu | Phe | Pro | Ile | His | Phe | Gly | Val | Ala | Ala | Lys | Asp |
| | | 35 | | | | | 40 | | | | | 45 | | | |
| Gln | Asp | Leu | Lys | Ser | Arg | Pro | Glu | Ser | Val | Glu | Cys | Ile | Arg | Tyr | Asn |
| | 50 | | | | | 55 | | | | | 60 | | | | |
| Phe | Arg | Gly | Phe | Arg | Trp | Leu | Gln | Ala | Met | Ile | Phe | Ala | Ile | Glu | Glu |
| 65 | | | | | 70 | | | | | 75 | | | | 80 | |
| Ile | Asn | Ser | Ser | Pro | Ala | Leu | Leu | Pro | Asn | Leu | Thr | Leu | Gly | Tyr | Arg |
| | | | | 85 | | | | | 90 | | | | | 95 | |
| Ile | Phe | Asp | Thr | Cys | Asn | Thr | Val | Ser | Lys | Ala | Leu | Glu | Ala | Thr | Leu |
| | | | 100 | | | | | 105 | | | | | 110 | | |
| Ser | Phe | Val | Ala | Gln | Asn | Lys | Ile | Asp | Ser | Leu | Asn | Leu | Asp | Glu | Phe |
| | | 115 | | | | | 120 | | | | | 125 | | | |
| Cys | Asn | Cys | Ser | Glu | His | Ile | Pro | Ser | Thr | Ile | Ala | Val | Val | Gly | Ala |
| | 130 | | | | | 135 | | | | | 140 | | | | |
| Thr | Gly | Ser | Gly | Val | Ser | Thr | Ala | Val | Ala | Asn | Leu | Leu | Gly | Leu | Phe |
| 145 | | | | | 150 | | | | | 155 | | | | 160 | |
| Tyr | Ile | Pro | Gln | Val | Ser | Tyr | Ala | Ser | Ser | Ser | Arg | Leu | Leu | Ser | Asn |
| | | | | 165 | | | | | 170 | | | | | 175 | |
| Lys | Asn | Gln | Phe | Lys | Ser | Phe | Leu | Arg | Thr | Ile | Pro | Asn | Asp | Glu | His |
| | | | 180 | | | | | 185 | | | | | 190 | | |
| Gln | Ala | Thr | Ala | Met | Ala | Asp | Ile | Ile | Glu | Tyr | Phe | Arg | Trp | Asn | Trp |
| | | 195 | | | | | 200 | | | | | 205 | | | |
| Val | Gly | Thr | Ile | Ala | Ala | Asp | Asp | Tyr | Gly | Arg | Pro | Gly | Ile | Glu | |
| | 210 | | | | | 215 | | | | 220 | | | | | |
| Lys | Phe | Arg | Glu | Glu | Ala | Glu | Glu | Arg | Asp | Ile | Cys | Ile | Asp | Phe | Ser |
| 225 | | | | | 230 | | | | | 235 | | | | 240 | |
| Glu | Leu | Ile | Ser | Gln | Tyr | Ser | Asp | Glu | Glu | Glu | Ile | Gln | His | Val | Val |
| | | | | 245 | | | | | 250 | | | | | 255 | |
| Glu | Val | Ile | Gln | Asn | Ser | Thr | Ala | Lys | Val | Ile | Val | Val | Phe | Ser | Ser |
| | | | 260 | | | | | 265 | | | | | 270 | | |
| Gly | Pro | Asp | Leu | Glu | Pro | Leu | Ile | Lys | Glu | Ile | Val | Arg | Arg | Asn | Ile |
| | | 275 | | | | | 280 | | | | | | 285 | | |
| Thr | Gly | Lys | Ile | Trp | Leu | Ala | Ser | Glu | Ala | Trp | Ala | Ser | Ser | Ser | Leu |
| | | 290 | | | | 295 | | | | | 300 | | | | |
| Ile | Ala | Met | Pro | Gln | Tyr | Phe | His | Val | Val | Gly | Gly | Thr | Ile | Gly | Phe |
| 305 | | | | | 310 | | | | | 315 | | | | 320 | |
| Ala | Leu | Lys | Ala | Gly | Gln | Ile | Pro | Gly | Phe | Arg | Glu | Phe | Leu | Lys | Lys |
| | | | | 325 | | | | | 330 | | | | | 335 | |
| Val | His | Pro | Arg | Lys | Ser | Val | His | Asn | Gly | Phe | Ala | Lys | Glu | Phe | Trp |
| | | | 340 | | | | | 345 | | | | | 350 | | |
| Glu | Glu | Thr | Phe | Asn | Cys | His | Leu | Gln | Glu | Gly | Ala | Lys | Gly | Pro | Leu |
| | | 355 | | | | | 360 | | | | | 365 | | | |
| Pro | Val | Asp | Thr | Phe | Leu | Arg | Gly | His | Glu | Glu | Ser | Gly | Asp | Arg | Phe |
| | | 370 | | | | 375 | | | | | 380 | | | | |
| Ser | Asn | Ser | Ser | Thr | Ala | Phe | Arg | Pro | Leu | Cys | Thr | Gly | Asp | Glu | Asn |
| 385 | | | | | 390 | | | | | 395 | | | | 400 | |
| Ile | Ser | Ser | Val | Glu | Thr | Pro | Tyr | Ile | Asp | Tyr | Thr | His | Leu | Arg | Ile |
| | | | | 405 | | | | | 410 | | | | | 415 | |
| Ser | Tyr | Asn | Val | Tyr | Leu | Ala | Val | Tyr | Ser | Ile | Ala | His | Ala | Leu | Gln |
| | | | 420 | | | | | 425 | | | | | 430 | | |
| Asp | Ile | Tyr | Thr | Cys | Leu | Pro | Gly | Arg | Gly | Leu | Phe | Thr | Asn | Gly | Ser |

10002354-110101

| | | | | | | | | | | | | | | | | |
|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|--|
| | | 435 | | | | | 440 | | | | | 445 | | | | |
| Cys | Ala | Asp | Ile | Lys | Lys | Val | Glu | Ala | Trp | Gln | Val | Leu | Lys | His | Leu | |
| | 450 | | | | | 455 | | | | | 460 | | | | | |
| Arg | His | Leu | Asn | Phe | Thr | Asn | Asn | Met | Gly | Glu | Gln | Val | Thr | Phe | Asp | |
| 465 | | | | | 470 | | | | | 475 | | | | | 480 | |
| Glu | Cys | Gly | Asp | Leu | Val | Gly | Asn | Tyr | Ser | Ile | Ile | Asn | Trp | His | Leu | |
| | | | | 485 | | | | | 490 | | | | | 495 | | |
| Ser | Pro | Glu | Asp | Gly | Ser | Ile | Val | Phe | Lys | Glu | Val | Gly | Tyr | Tyr | Asn | |
| | | | 500 | | | | | 505 | | | | | 510 | | | |
| Val | Tyr | Ala | Lys | Lys | Gly | Glu | Arg | Leu | Phe | Ile | Asn | Glu | Glu | Lys | Ile | |
| | | 515 | | | | | 520 | | | | | 525 | | | | |
| Leu | Trp | Ser | Gly | Phe | Ser | Arg | Glu | Val | Pro | Phe | Ser | Asn | Cys | Ser | Arg | |
| | 530 | | | | | 535 | | | | | 540 | | | | | |
| Asp | Cys | Leu | Ala | Gly | Thr | Arg | Lys | Gly | Ile | Ile | Glu | Gly | Glu | Pro | Thr | |
| 545 | | | | | 550 | | | | | 555 | | | | | 560 | |
| Cys | Cys | Phe | Glu | Cys | Val | Glu | Cys | Pro | Asp | Gly | Glu | Tyr | Ser | Asp | Glu | |
| | | | | 565 | | | | | 570 | | | | | 575 | | |
| Thr | Asp | Ala | Ser | Ala | Cys | Asn | Lys | Cys | Pro | Asp | Asp | Phe | Trp | Ser | Asn | |
| | | | 580 | | | | | 585 | | | | | 590 | | | |
| Glu | Asn | His | Thr | Ser | Cys | Ile | Ala | Lys | Glu | Ile | Glu | Phe | Leu | Ser | Trp | |
| | | 595 | | | | | 600 | | | | | 605 | | | | |
| Thr | Glu | Pro | Phe | Gly | Ile | Ala | Leu | Thr | Leu | Phe | Ala | Val | Leu | Gly | Ile | |
| | 610 | | | | | 615 | | | | | 620 | | | | | |
| Phe | Leu | Thr | Ala | Phe | Val | Leu | Gly | Val | Phe | Ile | Lys | Phe | Arg | Asn | Thr | |
| 625 | | | | | 630 | | | | | 635 | | | | | 640 | |
| Pro | Ile | Val | Lys | Ala | Thr | Asn | Arg | Glu | Leu | Ser | Tyr | Leu | Leu | Leu | Phe | |
| | | | | 645 | | | | | 650 | | | | | 655 | | |
| Ser | Leu | Leu | Cys | Cys | Phe | Ser | Ser | Ser | Leu | Phe | Phe | Ile | Gly | Glu | Pro | |
| | | | 660 | | | | | 665 | | | | | 670 | | | |
| Gln | Asp | Trp | Thr | Cys | Arg | Leu | Arg | Gln | Pro | Ala | Phe | Gly | Ile | Ser | Phe | |
| | | 675 | | | | | 680 | | | | | 685 | | | | |
| Val | Leu | Cys | Ile | Ser | Cys | Ile | Leu | Val | Lys | Thr | Asn | Arg | Val | Leu | Leu | |
| | 690 | | | | | 695 | | | | | 700 | | | | | |
| Val | Phe | Glu | Ala | Lys | Ile | Pro | Thr | Ser | Phe | His | Arg | Lys | Trp | Trp | Gly | |
| 705 | | | | | 710 | | | | | 715 | | | | | 720 | |
| Leu | Asn | Leu | Gln | Phe | Leu | Leu | Val | Phe | Leu | Cys | Thr | Phe | Met | Gln | Ile | |
| | | | | 725 | | | | | | 730 | | | | 735 | | |
| Val | Ile | Cys | Val | Ile | Trp | Leu | Tyr | Thr | Ala | Pro | Pro | Ser | Ser | Tyr | Arg | |
| | | | 740 | | | | | 745 | | | | | 750 | | | |
| Asn | Gln | Glu | Leu | Glu | Asp | Glu | Ile | Ile | Phe | Ile | Thr | Cys | His | Glu | Gly | |
| | | 755 | | | | 760 | | | | | | 765 | | | | |
| Ser | Leu | Met | Ala | Leu | Gly | Phe | Leu | Ile | Gly | Tyr | Thr | Cys | Leu | Leu | Ala | |
| | 770 | | | | | 775 | | | | | 780 | | | | | |
| Ala | Ile | Cys | Phe | Phe | Phe | Ala | Phe | Lys | Ser | Arg | Lys | Leu | Pro | Glu | Asn | |
| 785 | | | | | 790 | | | | | 795 | | | | | | |

| | | | | |
|---|------|------|------|------|
| 930 | | 935 | | 940 |
| Gln Gln Pro Leu Thr Leu Pro Gln Gln Gln Arg Ser Gln Gln Gln Pro | | | | |
| 945 | | 950 | | 955 |
| Arg Cys Lys Gln Lys Val Ile Phe Gly Ser Gly Thr Val Thr Phe Ser | | | | |
| | 965 | | 970 | 975 |
| Leu Ser Phe Asp Glu Pro Gln Lys Asn Ala Met Ala His Arg Asn Ser | | | | |
| | 980 | | 985 | 990 |
| Thr His Gln Asn Ser Leu Glu Ala Gln Lys Ser Ser Asp Thr Leu Thr | | | | |
| | 995 | 1000 | | 1005 |
| Arg His Gln Pro Leu Leu Pro Leu Gln Cys Gly Glu Thr Asp Leu Asp | | | | |
| | 1010 | 1015 | | 1020 |
| Leu Thr Val Gln Glu Thr Gly Leu Gln Gly Pro Val Gly Gly Asp Gln | | | | |
| 1025 | | 1030 | | 1035 |
| Arg Pro Glu Val Glu Asp Pro Glu Glu Leu Ser Pro Ala Leu Val Val | | | | |
| | 1045 | | 1050 | 1055 |
| Ser Ser Ser Gln Ser Phe Val Ile Ser Gly Gly Gly Ser Thr Val Thr | | | | |
| | 1060 | 1065 | | 1070 |
| Glu Asn Val Val Asn Ser | | | | |
| 1075 | | | | |

1002254 "110101